UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/819,946	03/28/2001	D. Wade Walke	LEX-0157-USA	2952

24231 7590 05/05/2004

LEXICON GENETICS INCORPORATED
8800 TECHNOLOGY FOREST PLACE
THE WOODLANDS, TX 77381-1160

EXAMINER	
BRANNOCK, MICHAEL T	
ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 05/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

UNITED STATES PATENT AND TRADEMARK OFFICE

COMMISSIONER FOR PATENTS
UNITED STATES PATENT AND TRADEMARK OFFICE
P.O. BOX 1450
ALEXANDRIA, VA 22313-1450
www.uspto.gov

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 042604

Application Number: 09/819,946
Filing Date: March 28, 2001
Appellant(s): WALKE ET AL.

Lance K. Ishimoto
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 11/14/03.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The Appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The Appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

Claims 1-3, 6 and 7 stand or fall together, as indicated by Appellant.

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

No prior art is relied upon by the examiner in the rejection of the claims under appeal.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 1-3, 6 and 7 stand rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. The claims are directed to polynucleotides of SEQ ID NO: 1 encoding polypeptides of SEQ ID NO: 2 The instant specification puts forth that the polypeptide is useful in a screening method to determine what ligands may activate or inhibit the polypeptide and also to determine what the physiological effects of the polypeptide might be (see page 1 and 4, for example). This proposed use lacks a specific and substantial utility. It is not a specific use because any integral membrane protein could be used in exactly the same way. Further, many polypeptides are known in the art, yet the polypeptides have no known function or known ligands. Any of these orphan clones could be used in the manner described in the specification for the claimed polypeptide.

Furthermore, the proposed use of the polypeptide to screen for ligands of the polypeptide or for biologic effects of the polypeptide is not a substantial utility. A substantial utility is a practical use which amounts to more than a starting point for further research and investigation and does not require or constitute carrying out further research to identify or reasonably confirm what the practical use might ultimately be. For example, an assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would be a practical use of the material. However, a method of treating an unspecified disease or condition with a material that has no particular correlation with a disease would not constitute a substantial utility. Basic research, such as studying the properties of the

claimed product or the mechanisms in which the product is involved, does not constitute a substantial utility.

The specification puts forth that the polypeptide could be involved in any number of disparate disease states, and could therefore be used as a diagnostic (page 6 and 33, for example) or therapeutic agent (see page 7 and 18, for example). A stated belief that a correlation exists between the polypeptides and any number of diseases is not sufficient guidance to use the claimed polynucleotides to treat and/or diagnosis a particular disease; it merely defines a starting point for further research and investigation.

The specification puts forth that the polynucleotides and polypeptides could be used as tissue specific or chromosomal markers, page 10. Consistent with current examination guidelines, use as a tissue specific and/or chromosomal marker is not considered to be a substantial utility. Most every polypeptide exhibits some tissue specific pattern of expression and most every gene encoding a polypeptide is localized to some region of a chromosome. However, without some assertion that the tissue or chromosomal localization can be used to practice a particular substantial utility, as in a marker for a particular disease state, the use of the polypeptides or polynucleotides as tissue or chromosomal marker does not constitute a substantial utility.

The specification puts forth that the polypeptide and/or polynucleotides could be used in forensic biology (page 37). However the specification does not teach that any particular nucleic acid or amino acid sequence is distinctive of any individual. While one of skill in the art would appreciate that there may exist polymorphisms in the disclosed sequences, this amounts to

nothing more than an invitation to the skilled artisan to try and find such polypmorphisms if they exist and then to try to determine if there is any significance related to them.

The specification states that the polypeptide has similarity to known taste, pheromone, calcium sensing, peptide hormone, and glutamate receptors (page 5), however the specification does not appear to assert that the polypeptide has any particular functional properties. Thus, there is no particular assertion of a use based on a particular functional property. The specification asserts that the polypeptide or polynucleotide could be used as part of a micro-array for toxicology testing, drug screening, and pharmacogenomics (see pages 11 and 14). These purposed uses are not substantial utilities because each use amounts to no more than an invitation to study the properties of the polynucleotide or polypeptides, e.g. to determine whether a compound alters the expression of the polypeptide, and then to determine what, if any, the consequence of that alteration may be, or also to determine what ligands might bind to the polypeptide, e.g. drug screening. Such an invitation to perform research on the claimed polynucleotide is not a substantial utility.

The instant application has failed to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a specific or substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed nucleic acids.

Claims 1-3, 6 and 7 are also rejected under 35 U.S.C. § 112 first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know

how to use the claimed invention so that it would operate as intended without undue experimentation.

(11) Response to Argument

At page 4 of the Brief, Appellant argues that Appellants have described a novel human taste receptor(TASR1), a protein of known function. This argument has been fully considered but not deemed persuasive. The instant application, which is the subject of appeal, does not assert that the polypeptide of SEQ ID NO: 2 is a taste receptor; the specification merely indicates that SEQ ID NO: 2 and several other proteins are similar to known taste, pheromone, calcium sensing, peptide hormone, and glutamate receptors (page 5), however the specification does not assert that the polypeptide of SEQ ID NO: 2 has any particular functional properties. That the polypeptide of SEQ ID NO: 2 is one half of a heterodimer that forms a sweet taste receptor was discovered by others several years after the filing of the instant specification. This work, cited by Appellant, cannot validate an assertion that SEQ ID NO: 2 is a taste receptor because no such assertion was made in the instant application; and nor was there any assertion that the polypeptide of SEQ ID NO: 2 was involved with any particular disease, disorder, or any other particular phenotype.

At page 5 of the Brief, Appellant argues that the protein's close similarity to known taste receptors in genetic databases (Exhibit A) clearly established that those of skill in the art would recognize the sequences of the present polypeptide as a human GPCR and a taste receptor. This argument has been fully considered but not deemed persuasive. First, it has never been disputed that one of skill in the art would recognize that the protein is a GPCR as there was much general

knowledge about GPCR structure at the time of filing; it is quite another matter, however, to say that a particular GPCR is a taste receptor. It is important to note that each of the examples in Exhibit A represent the results of considerable research effort to determine if particular GPCRs were taste receptors, and none of these results was available at the time of filing of the instant application.

Second, knowledge that the polypeptide is a taste receptor does not provide the artisan with sufficient knowledge as to how to immediately use the polypeptide in any way that provides a substantial utility. Using the information provided by instant disclosure and by the prior art, the artisan might then begin a research plan to determine what particular properties the protein has, e.g. to try to find what tastants bind to the protein, or determine how the protein is involved in the perception of taste, so as to ultimately learn how to use the protein. The specification provides no guidance as to how to use the protein based on any property relating to taste. The specification merely asserts that the polypeptide has homology to known receptors having disparate functions and properties, e.g. taste, pheromone, calcium sensing, peptide hormone, and glutamate receptors (page 5). Thus, the question at issue is whether or not the broad general assertion that the claimed nucleic acids might be used for *some* diagnostic application in the absence of a disclosure of *which* diagnostic application would be considered to be an assertion of a specific, substantial, and credible utility. For reasons set forth above the disclosure satisfies none of the three criteria *See In re Kirk*, 153 USPQ 48, 53 (CCPA 1967) (quoting the Board of Patent Appeals, 'We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an Appellant could satisfy the requirements of the statutes by indicating the usefulness of a claimed

compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.'

At page 6 of the Brief, Appellant argues the instant polynucleotides encode a GPCR and that most drugs target GPCRs, thus membership in the group of GPCRs confers a specific, substantial credible well-established utility. The specification has not asserted a utility that is specific to the instant molecule, the asserted utilities are based on any use that is common to all members of the GPCR family, yet importantly, there does not appear to be any particular use, common among the GPCR family members, that amounts to a substantial utility. There does not appear to be a common property that GPCRs share, and that any new member might also be expected to possess, that could be exploited in a manner that could be considered a substantial utility under 35 U.S.C. § 101. Each asserted use, e.g. drug screening, expression profiling, toxicology testing, etc., being based on the common properties of GPCRs, amounts to no more than an invitation to the skilled artisan to take the polypeptides and try to find if any drugs bind the polypeptides, or try to find any correlation between the expression of the polypeptides and the administration of any particular drug, or to see if there is a correlation between the expression of the polypeptides and the onset of any particular disease. While this type of multi-million dollar basic research is recognized in the "real world" it cannot, alone, be the basis of a patent. Appellants asserted utilities are essentially a call to perform such research and investigation; and, as set forth previously, such basic research as studying the properties of the claimed product or the mechanisms in which the product is involved does not constitute a substantial utility. Thus,

the asserted utilities are not specific to the claimed molecules and nor are the utilities substantial because each requires extensive experimentation to try to find a way, ultimately, to use the molecules.

Appellant's arguments in the last paragraph of page 6, regarding comparisons between the instant Application and issued patents have been fully considered but are not persuasive. The examiner is unaware of any requirement that examination of the instant Application for utility and enablement should include any comparison to an issued patent.

At page 7 of the Brief, Appellant argues that the polypeptide and the fact pattern of the instant invention are most like that of Example 10 of the Revised Interim Utility Guidelines, in that the instant polypeptide is a taste receptor and that the utility of the present claims is based on the well-established utility of taste receptors. This argument has been fully considered but not deemed persuasive. In Example 10 of the guidelines, the specification *asserts* that the claimed polypeptide is a DNA Ligase. One of skill in the art could then reasonably conclude that the *particular* substrates for the claimed polypeptide are DNA and ATP, and would also know how to *specifically* use the polypeptide e.g. to ligate DNA, without having to perform experimentation to find a way to use the polypeptide. The specification has not asserted that the claimed polypeptide binds to any *particular* ligand or is in anyway involved in the perception of taste. The performance of further research and investigation in order to determine what ligand or what particular properties the protein may have is not considered to be a specific or otherwise substantial utility.

At page 8 of the Brief, Appellant argues that recent evidence supports the assertion that the protein is a taste receptor and is therefore a legitimate target of the drug discovery process.

This argument has been fully considered but not deemed persuasive. There is no disagreement that the protein has subsequently been found to be a taste receptor. The issue is that specification did not assert that the polypeptide was a taste receptor, and merely presented the invitation to try to find out what type of receptor it was. This does not constitute a substantial utility.

Appellant's arguments regarding DNA chips and microarrys on page 9 of the Brief have been fully considered but not deemed persuasive. The skilled artisan understands that the specification has merely presented an invitation to use microarray technology to study the expression patterns of the claimed polynucleotide, e.g. to see if the expression changes in response to a drug and to then try to determine if such a change has any meaningful consequence. As set forth previously, such a use does not constitute as specific or otherwise substantial utility.

At page 9 of the Brief, Appellant argues that the examiner appears to be requiring that Appellants identify the biological role or function of the protein; and also that Appellants have indeed identified the biological role. This argument has been fully considered but not deemed persuasive. There is no such requirement that *the* biological role or *the* function of the protein be disclosed or explained. The issue is that the specification failed to provide any property of the polypeptide that could be used in a way other than as an object for further research and investigation to try to find some particular property that could be exploited in a way that would constitute a specific or otherwise substantial utility. That such a property, e.g. a receptor for sweet taste perception, was found by others several years after the filing of the instant application is irrelevant to the instant appeal.

At pages 9 and 10 of the Brief, Appellant argues that the use of polynucleotides and polypeptides, such as that of the instant invention, is well established in the field of microarray technology (e.g. gene chips). This argument has been fully considered but not deemed persuasive. It is agreed that microarray technology has patentable utility. However, the microarray is not being claimed, but rather a polynucleotide that can be used in microarrays. The claimed polynucleotide is not disclosed as being expressed at an altered level or form in any diseased tissue as compared to the corresponding healthy tissue. The claimed polynucleotide is not disclosed as being expressed at an altered level or form under any set of conditions or being correlated with any particular phenotype. Nor has there been any assertion of any particular effect or outcome that may be discerned from the presence of the polynucleotide in a gene chip. Therefore, the assertion that the claimed polynucleotide has patentable utility as a probe in, or member of, a microarray is not specific. Any orphan polynucleotide can be used in the same way.

Appellant refers to other publications and patents that discuss microarrays and gene expression technology with respect to drug screening and toxicology testing. Again, this is not found to be persuasive, because the arguments and evidence merely show that microarray technology is important and useful to the scientific community. These publications do not show that the claimed invention has a patentable utility. The use of the claimed uncharacterized polynucleotides in such studies would have provided no more information than the use of any other polynucleotide encoding an orphan protein. The asserted utility for the claimed polynucleotide is not specific to the claimed polynucleotide. Due to the lack of disclosure of a

correlation between the claimed polynucleotides and a particular disorder, or any particularly useful phenotype, the asserted utility is also not substantial, as discussed above.

At pages 10-11 of the Brief, Appellant argues, essentially, that any polynucleotide known to comprise an exon would have credible and substantial utility in the analysis of genomic data. Again, this is a utility which would apply to virtually ever member of a general class of materials, such as any collection of proteins. Neither Appellant's cited references nor the instant specification appear to assert a use that amounts to a substantial utility. The skilled artisan appreciates that Appellant's asserted uses for the polynucleotide, e.g. in the analysis of how the gene is transcribed and/or organized is simply a study of the properties of the claimed nucleic acid. As set forth previously, such basic research as studying the properties of the claimed product or the mechanisms in which the product is involved does not constitute a substantial utility.

Appellant argues, essentially, that a "real-world" utility exists if actual use or commercial success can be shown. Citing case law, Appellant argues that thousands of venture capitalists and the scientific community have acknowledged the value genomic data, and that databases that included the claimed polynucleotide would be even more valuable. Appellant's arguments have been fully considered but are not deemed to be persuasive. The case law indicates that a rejection under 35 U.S.C. § 101 *for lack of operability* can be overcome by a showing of actual use or commercial success. The instant issue is whether or not the asserted utilities meet the three-pronged test for credibility, specificity, and substantiality. Such is not necessarily addressed by a showing of commercial success or actual use. Many products which lack patentable utility enjoy commercial success, are actually used, and are considered valuable.

These include silly fads such as pet rocks, but also include serious scientific products like orphan receptors.

At page 11 of the Brief, Appellant argues the disclosure of polymorphisms enables the artisan to use the polynucleotides in forensic analysis. This argument has been fully considered but not deemed persuasive. The issues are (1) that the specification does not teach that any particular nucleic acid or amino acid sequence is distinctive of any individual. (2)While one of skill in the art would appreciate that there may exist polymorphisms in the disclosed sequences, this amounts to nothing more than an invitation to the skilled artisan to try and find such polypmorphisms and then to determine any consequence of these polymorphisims. This use is not specific because any naturally occurring polynucleotide could be used in the same way. It is not substantial because it is simply an invitation to try to find polymorphisms and then to try to find correlations between them and any phenomena. (3) Additionally, as set forth previously, it is unclear it the polymorphisms disclosed in the specification are naturally occurring or are artifacts of the cloning and sequencing procedures. The skilled artisan would therefore appreciate that the instant disclosure of such polymorphisms simply presents an invitation to the artisan to investigate the claimed polynucleotides to try to determine if such polymorphisms are indicative of any human individual or of any phenomena that could be further exploited.

Additionally, Appellant argues that even in the "worst case scenario" the described polymorphisms are each useful to distinguish 50% of the population. The examiner admits that he may not entirely understand Appellant's reasonings, however the issue remains that the specification does not teach that any particular nucleic acid or amino acid sequence is distinctive of any individual.

At pages 11-13 of the Brief, Appellant argues that the use of the polynucleotides as polymorphic markers is a specific utility. This argument has been fully considered but not deemed persuasive. The instant fact pattern is indistinguishable from that example provided in the REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS as indicated to not qualify as a specific utility:

"Specific utility "– A utility that is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe "or "chromosome marker" would not be considered to be specific in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed.

Thus it is appreciated that any naturally occurring polynucleotide has a location on a chromosome, however, without some assertion that the tissue or chromosomal localization can be used to practice a particular utility that is specific to that polynucleotide , such as in a marker for a particular disease state, the use of the polypeptides or polynucleotides as tissue or chromosomal markers does not constitute a specific or otherwise substantial utility.

Beginning at page 13 of the Brief, Appellant argues that the claimed polynucleotide sequences have utility in "determining the genomic structure", "identification of protein coding sequence", and "identification of exon splice junctions" and provide biologically validated empirical data that specifically define that portion of the corresponding genomic locus that actually encodes exon sequence. Appellant newly cites the Venter reference to allegedly demonstrate the significance of expressed sequence information in the structural analysis of genomic data. This has been fully considered but is not deemed to be persuasive because such a utility is considered a research utility, only designed to identify a particular function of the

claimed sequences and is not a substantial utility. See, e.g., Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966) wherein a research utility was not considered a "substantial utility." While the Examiner agrees with the Appellant on the scientific value of the claimed polynucleotide sequences and on the significance of expressed sequence information in structural analysis of genomic data, such a use of the polynucleotide sequences in gene mapping does not represent a specific and substantial utility. The exhibit and the publication cited by the Appellant merely show that the significance of expressed sequences in the structural analysis of genomic data; they do not show that the present polynucleotide sequences have a patentable utility.

On pages 13-15 of the Brief, Appellant summarizes case law on the utility requirement. Citing case law, Appellant urges that the present claims clearly meet the requirement of 35 U.S.C. §101. The essential disagreement appears to be the interpretation of what constitutes a specific, substantial and credible utility.

Appellant's arguments have been fully considered but are not deemed to be persuasive for the following reasons. First, the statement, "(t)o violate §101 the claimed device must be totally incapable of achieving a useful result." Brooktree Corp. v. Advanced Micro Devices, Inc., 977 F.2d 1555, 1571, 24 USPQ2d 1401 (Fed. Cir. 1992), indicates that a rejection under 35 U.S.C. § 101 for lack of operability can be overcome by a showing of actual use or commercial success. The claimed invention in the instant case is drawn to nucleic acid sequences, not a device; the instant rejection under 35U.S.C. §101 is not directed to inoperativeness of a device, rather to a lack of patentable utility of the claimed nucleic acid sequences; and the instant issue is whether the asserted utilities meet the three-pronged test for a patentable utility.

Secondly, since the specification fails to disclose a specific, substantial utility or a well-established utility, the present claims do not satisfy the utility requirement of 35 U.S.C. §101. Merely citing case laws on the utility requirement does not render a patentable utility for the present invention. While "anything under the sun that is made by man" is patentable, it does not mean everything under the sun that is made by man meets the statutes of 35 U.S.C. §101. In fact, the present invention is not patentable due to lack of a patentable utility.

Appellant's reliance on *In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995) is misplaced. That court decision determined that a compound which belonged to a family of compounds known to have anti-tumor activity, which is a common and well established utility for that family of compounds, would be reasonably expected to have anti-tumor activity in light of positive in vitro data with respect to that particular compound since that data has proven to be an indicator of anti-cancer activity by other members of that family. As indicated above, the protein of the instant invention does not belong to a family of compounds with a *common* well established specific and substantial utility. The utility of a particular member of the receptor family, to which the protein in the instant application belongs, lies in the knowledge that the particular member modulates a specific physiological activity in response to a specific ligand or is involved in a particular disease or some other phenotype. Since the instant specification does not disclose the identity of a native ligand for the instant protein nor the identity of the pathway through which that receptor transduces it signal in response to that ligand, nor any other particular phenotype associated with the polynucleotide or the protein, the instant claimed polynucleotide is not particularly useful other than as an object for further research.

Appellant argues from the stand point that the requirement for some experimentation to practice the invention does not negate the utility requirement. This argument has been fully considered but not deemed persuasive. The issue is not that some experimentation is required to use the polypeptide in a particular asserted way; the issue is that, in the instant case, experimentation is required to try to find a way to particularly use the polypeptide, such experimentation, itself, being the asserted use and also being merely a starting point for research and investigation. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." Brenner v. Manson, 148 USPQ at 696. Thus, the disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. §101.

Appellant's arguments, at pages 16-18 regarding due process and comparisons between the instant application and issued patents have been fully considered but are not persuasive. The examiner is unaware of any requirement that examination of the instant Application for utility and enablement should include a comparison to an issued patent. Regarding the promulgation of the current examination guidelines, a Primary Examiner has no authority to comment on the legality of the examination guidelines nor on the validity of an issued US patent. Thus, such an issue should be reserved for ruling by the Board of Patent Appeals and Interferences.

Appellant concludes this section by urging that the rejection of claims 1-3, 6 and 7 under 35 U.S.C. § 101 must be overruled. The Examiner believes that the rejections should be sustained for the reasons set forth above.

B. Are claims 1-3, 6 and 7 unpatentable due to a lack of enabling disclosure?

As Appellant indicates at page 18 of the Brief, a rejection under U.S.C. § 112, first paragraph, may be affirmed on the same basis as a lack of utility rejection under 35 U.S.C. § 101.

Therefore, for reasons set forth above, Appellant's arguments and exhibits have been fully and carefully considered, but are not considered sufficient to rebut the prima facie case of lack of utility. For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Michael Brannock, Ph.D.
Examiner
Art Unit 1646

MB

April 28, 2004

Conferees:

Yvonne Eyler, Ph.D.
SPE, Technology Center 1600

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Anthony Caputa, Ph.D.
Practice Specialist, Technology Center 1600

LEXICON GENETICS INCORPORATED
8800 TECHNOLOGY FOREST PLACE
THE WOODLANDS, TX 77381-1160